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BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

Original Articles

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CENTENNIAL CELEBRATION

1847—CENTENNIAL OF THE ACADEMY—1947

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THE NEW YORK ACADEMY
OF MEDICINE

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CENTENNIAL CELEBRATION

1847 – 1947

As The New York Academy of Medicine enters its second century of service to the medical profession and to the public, it will review the achievements of its stalwarts of the past and Janus-like, look forward with eager eyes to the opportunities and problems which will confront this changing world. The strength of the Academy has developed from a twofold source–its men and its forthright attitude and purpose. Its men have been strong and its purpose that of service and leadership.

The programs of the Sections will exemplify this bifocal function of the Centennial Celebration and it is hoped that, aside from addresses on specific techniques or problems in medicine, the members of the Sections will grasp this opportunity to survey the past and look into the immediate future in the various fields of medicine, surgery, and psychiatry.

A glance at the programs for the Institutes on Social Medicine, Public Health, and Medical Education suggests the interest and the responsibilities of the Academy in some of the broader fields of medical activity, fields often touched by the individual physician only with difficulty, and only if he is minded that way. These Institutes will be working conferences devoted to the subjects indicated and led by acknowledged leaders in the respective fields. The Institutes will be conducted informally and should prove to be both expository and pro-

vocative. The Institute on Library has been planned to be of help to medical library workers in dealing with some of their working problems. However, some of the particular items on its program may well fall within the field of interest of many of the Fellows, whether in the use of medical libraries or the accumulation and arrangement of their own book collections. This is a splendid opportunity to become reacquainted with the Academy Library.

It is with great pleasure that the Academy welcomes the participation of its affiliated societies which are presenting programs in keeping with the spirit of the Centennial Celebration. The New York Academy of Sciences will hold its Saturday Conference on March twenty-second at the Academy of Medicine building. The program deals with problems of the adrenals.

The Hospital Council of Greater New York will also coöperate by holding a three-day Institute on Hospitals and by presenting an exhibit in Room A during March and April. The exhibit will illustrate hospital plans and projects particularly in this geographic area which will interest all of the profession. In addition, it is proposed that the Council's Master Plan for Greater New York will be shown for the first time.

Extensive exhibits of museum material, old and rare books, manuscripts, portraits, and prints, will be shown in the Academy building. It is also of interest that concurrent exhibits of a medical nature may be viewed at several other institutions, notably the Metropolitan Museum of Art, the Museum of the City of New York, and the New York Historical Society. The Academy appreciates the coöperation of these institutions.

The Centennial Dinner on March sixth at the Waldorf-Astoria will be addressed by the President of the Academy, by representatives of Government, and by Dr. John A. Ryle, erstwhile Regius Professor of Physic at Cambridge University and at present the Head of the Institute of Social Medicine at Oxford.

Participation in the Centennial Celebration of The New York Academy of Medicine provides an opportunity which should be embraced by the Fellowship and friends of the Academy for the good of the Fellows, for the good of the public, and for the good of the Academy.

HOWARD REID CRAIG, *Director*

RECENT ADVANCES IN CANCER THERAPY*

C. D. HAAGENSEN

College of Physicians and Surgeons, Columbia University

FROM time to time it is useful to review in our own scientific circle the status of cancer therapy. The reports of "spectacular" therapeutic advances in the daily press are, unfortunately, not only unreliable but harmful. Progress in cancer therapy is not as dramatic as progress in cancer research. The laboratory worker, some fine morning in May, finds ten of his mice with tumors induced by nucleo-protein that he has prepared by careful precipitation and concentration, and he has a discovery. The clinician, on the other hand, compares, through a long period of years, the results of tedious and varied methods of treatment. His conclusions are based to a great degree upon the breadth of his experience and the soundness of his common sense, rather than upon close reasoning. He is often faced with a choice between two poor methods of treatment, and must take care at least to do no harm. Thus, I must ask your indulgence tonight if I state our therapeutic attitude in somewhat general terms, without documentation at every point.

It is of interest to review for a moment the history of our therapeutic attack on cancer. Looking backward fifty years to Halsted's day, we find the masters of surgery developing the techniques of the radical surgical attack on cancer. These courageous surgeons had many handicaps. One of the most serious was the lack of a practical method of immediate microscopical diagnosis. They had to rely on gross pathology which now and then betrayed them. And they had a distressingly high operative mortality. Surgery in those days was often truly heroic.

It is no wonder that many turned hopefully to radiation when it became generally available about twenty-five years ago. The deceptively favorable initial response to radiation of some types of cancer, such as epithelioma of the skin, raised almost everyone's hopes that radium or x-rays could be developed to the point of controlling most forms of

* Read at the opening evening session of the Nineteenth Graduate Fortnight of The New York Academy of Medicine, October 7, 1946.

cancer. A man of high idealism and great good will like James Ewing could carry on what amounted to a crusade for radiation. This wave of enthusiasm for radiation led to its use for all types of neoplasms, and the evolution of many ingenious methods of applying it.

Unfortunately, these high hopes of a generation ago in the curative value of radiation were dissipated as knowledge of its effects accumulated and the end results became available.

Today it is clear that except for a few types of cancer such as some forms of epithelioma of the skin, epithelioma of the larynx, and epithelioma of the cervix, radiation can not compete with surgery as a curative agent. This period of disillusionment in the curative value of radiation carried us into the 1930's, and the period preceding the recent war.

Although our experiments with radiation left many of us chastened, they taught us important lessons. First, they revealed the great usefulness of radiation as a palliative form of treatment. From this palliative standpoint alone radiation has won for itself an important and lasting place among the weapons which every properly equipped hospital must possess. Trained radiotherapeutists are an essential part of any organization attempting to treat cancer today. Radiation checks temporarily several types of malignant disease in which surgery is futile. Lymphoblastomas and the highly malignant epitheliomas of the posterior tongue and pharynx are examples. It brings relief to many suffering with metastases from breast cancer.

A second gain from our period of enthusiasm for radiation has been the development of specialization in cancer. It is a historical fact that the cancer clinics in which radiotherapy evolved, the Radium Institute in Paris, the Radiumhemmet in Stockholm, and our Memorial Hospital, have also become the leading centers for training specialists in cancer diagnosis and treatment. James Ewing was a firm believer in specialization in cancer and we can thank him for what progress has been made in gaining recognition for our specialty in this country.

As with most other modern complex fields of knowledge, specialization in cancer has been fruitful. It has led to improved diagnosis and more expert care of the patient. The public and a large section of the medical profession are well aware of this fact, and cancer hospitals and cancer clinics are handling a constantly increasing share of the cancer patients.

Despite all this the medical schools and teaching hospitals have not given our specialty much recognition. The academic mind continues to resist new forms of specialization despite the fact that the rapidly increasing complexity of modern science makes specialization as inevitable as tomorrow's sunrise. In any good hospital clinic on any day one sees a wide variety of specialists excelling in their knowledge of the diseases in which they are specially interested. A man who spends the mature years of his life studying one disease naturally comes to know more about it than his colleagues who dissipate their efforts. If he happens to be an able technician he develops a superior surgical technique. But his technical skill is the least important of his advantages. If he has had a broad general training before specializing, and if he is a man of intelligence, he will draw upon knowledge from the fundamental sciences and from every field of medicine and surgery and apply it in his intensive study of the disease in which he specializes. It is not just to stigmatize such a man as a narrow specialist in technique.

Although the traditional conservative point of view that the general surgeon can treat the various types of cancer equally well still prevails in academic circles, there are signs of a beginning awareness of the advantages of a degree of specialization in cancer. It is becoming apparent that the surgeon who ecels in abdominal surgery and is of necessity an expert in gastrointestinal physiology, may treat cancer of the stomach and bowel with great skill; yet he may not do as well with the tedious and radical dissections required for cancer occurring elsewhere in the body, for example in the mammary gland, where a knowledge of pathology is more fundamental. There is need for all our skills in dealing with such a formidable enemy as cancer, and no one man can encompass them all. Let us by all means aim first at what is best for the patient and forget tradition.

To continue our historical review we come to the present trend in cancer therapy. It might be called the surgical epoch. During the last ten or fifteen years advances in certain of the fundamental aspects of surgery have made it so much safer that it is today possible to attack cancer far more vigorously. Improved anesthesia today permits the surgeon to operate for a far longer period of time without excessive shock. Operating on the surface of the body we can work comfortably for five or six hours. This permits us to do much more thorough and better dissections. It is fair to say that this improvement in anesthesia

has been the most important single factor in the recent rapid development of thoracic surgery and the attack on lung cancer.

The improved facilities for blood transfusion have also been of much assistance to the surgeon in his attack on cancer, for they have certainly lowered the mortality from operative shock.

The abdominal surgeon has found a strong defence against his old enemy, intestinal obstruction, in the use of the Abbott tube. Abbott is gone, struck down himself by malignant disease, but his discovery is saving lives every day of patients who have had gastric or bowel resections for cancer.

The frequency of local recurrence following many types of operations for cancer that have been done in the past can leave no doubt about the desirability of surgeons taking advantage of their newly found technical advantages. Our course, indeed, is clear. In many forms of cancer where radiation has failed to cure or has given only a limited percentage of cures, and where a more radical surgical attack is possible, we must have the courage to develop it, no matter how mutilating it may be. This, we might say, is our present temper.

The surgeon who today faces the grave responsibility of carrying out a mutilating operation for cancer has one solid advantage over his predecessor of Dr. Halsted's era: he has the surgical pathologist by his side to assist him in making certain of the diagnosis and to advise him as to the extent of the dissection. Fifty years ago surgical pathologists did not exist and the frozen section method of making an immediate microscopic diagnosis had not been developed. It was, in fact, in 1905 that Wilson of the Mayo Clinic began to use it. Dr. Halsted and his contemporaries had to depend upon their clinical impressions and their knowledge of gross pathology in diagnosis. We know that every now and then, particularly for lesions of the mammary gland, these evidences are delusive. Dr. Bloodgood, as a matter of fact, once wrote in an account of his early days in Halsted's clinic that 10 per cent of the benign lesions of the breast were mistaken for carcinoma and radical mastectomy needlessly done.

Thanks to the methods of immediate microscopical diagnosis which surgical pathologists have since perfected, this kind of mistake need never occur today. The frozen section method of diagnosis is the one which Dr. Stout and I have found to be the most desirable, and we have no evidence that the careful excision for frozen section of a tiny

wedge of tissue measuring only a few millimeters in size, from the superficial aspect of the lesion, is harmful. Others prefer the aspiration method of diagnosis. No matter which method is used the surgical pathologist has rescued us surgeons from the sea of doubt and set our feet on solid ground.

Equally important is the fact that the surgical pathologist is our guide in planning the extent and the nature of our attack on cancer. His microscope is a measure of how it extends and metastasizes. A great many patients come for treatment so late that their lesions are inoperable, or to put it another way, surgery will do more harm than good. This decision depends primarily upon a knowledge of surgical pathology.

At Columbia, A. P. Stout, as surgical pathologist, Maurice Lenz, as radiotherapeutist, and John Hanford and I as surgeons, have formed a team in attacking cancer. We see the patients together in the outpatient Neoplasm Clinic, and advise regarding problems arising on the wards and in the operating room. We keep special records of certain types of cancer cases, and from time to time review our therapeutic results. In this kind of team each member must know a good deal about the other's specialty, if there is to be a genuine meeting of minds. The surgical pathologist should have been trained in clinical surgery, and the surgeons and the radiotherapeutists should have had an apprenticeship in surgical pathology.

There is today in this country a great shortage of surgical pathologists and of funds with which to pay them. They are keymen in a cancer clinic. Surgeons and radiotherapeutists gain their income from private practice, but the surgical pathologist is traditionally an employee of the hospital in which he serves, and his salary is notoriously inadequate. Hospitals in which there is no surgical teaching tend to skimp or do without pathology. Men of ambition and talent will be attracted to the specialty only when there is promise of better salaries. If I were asked today what single kind of subsidy on the part of the Federal government would do the most to improve cancer therapy throughout the country, I would say "A fund providing fellowships to train surgical pathologists, and adequate salaries for men properly trained in the specialty, in key hospitals in every community." The cancer clinics which are springing up everywhere now-a-days would be tremendously helped by this kind of subsidy for surgical pathologists.

CANCER

AVERAGE ANNUAL INCIDENCE RATES PER 100,000 POPULATION
NEW YORK STATE, EXCLUSIVE OF NEW YORK CITY
1942-1943-1944

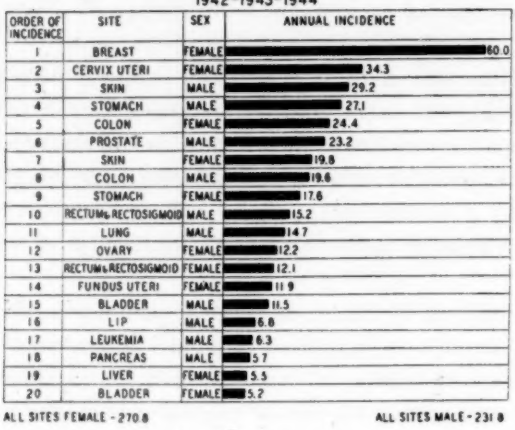
ORDER OF INCIDENCE
SITE
SEX
ANNUAL INCIDENCE
1 BREAST FEMALE 60.0
2 CERVIX UTERI FEMALE 34.3
3 SKIN MALE 29.2
4 STOMACH MALE 27.1
5 COLON FEMALE 24.4
6 PROSTATE MALE 23.2
7 SKIN FEMALE 19.8
8 COLON MALE 19.6
9 STOMACH FEMALE 17.6
10 RECTUM & RECTOSIGMOID MALE 15.2
11 LUNG MALE 14.7
12 OVARY FEMALE 12.2
13 RECTUM & RECTOSIGMOID FEMALE 12.1
14 FUNDUS UTERI FEMALE 11.9
15 BLADDER MALE 11.5
16 LIP MALE 6.8
17 LEUKEMIA MALE 6.3
18 PANCREAS MALE 5.7
19 LIVER FEMALE 5.5
20 BLADDER FEMALE 5.2
ALL SITES FEMALE - 270.8
ALL SITES MALE - 231.8

TABLE I

Having reviewed the general trend of cancer therapy it is of interest to speak briefly of the current view regarding the treatment of the most frequent special types of malignant disease, illustrating, as we go along, some of the general conclusions that we have drawn.

I should like first to call your attention to Table I which shows in graphic form the recent morbidity data for cancer in New York State compiled by Dr. Morton Levin of the State Department of Cancer Control. These data are unique, I believe. They have been collected with great care from hospitals, doctors, and public health agencies. They provide, for the first time, a fairly accurate picture of the true comparative incidence of the various types of cancer. This order of incidence is rather different than the impression which those of us who work entirely in hospitals have had. Cancer of the breast is by far the most frequent type, being almost twice as common as any other form of cancer. Cancer of the cervix is next in order, followed by cancer of the skin in males. Cancer of the stomach in males is fourth in order. Cancer of the colon in females is fifth, cancer of the prostate is sixth in order. Cancer of the skin in females is seventh. Cancer of the colon in males is eighth. Cancer of the stomach in females is ninth. Cancer

of the rectum and rectosigmoid in males is tenth. Cancer of the lung, which appears to be the only form of cancer that is actually increasing, is far more common in males than in females, and in our chart it is eleventh in order. Cancer of the ovary is twelfth. Cancer of the rectum and rectosigmoid in females is thirteenth, and cancer of the fundus of the uterus is fourteenth. Cancer of the bladder in males is fifteenth. The remaining forms of cancer are considerably less frequent, and need not occupy us here.

Cancer of the Breast

Cancer of the breast presents a diagnostic problem that requires expert clinical and pathological judgment. The public has been pretty well convinced that a tumor in the breast requires surgical investigation. Not so all doctors. There is appalling evidence that our medical education is not fitting physicians to meet this diagnostic problem. In a series of cases which we have recently studied from the viewpoint of who was responsible for the delay in diagnosis we found that the patient was to blame in 63 per cent of the cases, but some physician was to blame in 27 per cent. These cases are all ones in which the patient had discovered her own tumor and went for advice concerning it. She was told that it was harmless, or given some kind of placebo, or told to return for re-examination at a distant date. She was *not* told that she might have a cancer and that she must enter a hospital promptly for diagnosis and treatment. In this series of patients the consequent delay between the time the patient received the bad medical advice and the time correct treatment was begun averaged 59.6 weeks. We know that a delay of more than six months in cancer of the breast cuts the cure rate in half.

These facts force us to conclude that the most important thing that we can do to improve results in cancer of the breast is to pound into our students and interns the simple and fundamental rule that any tumor of the breast, no matter how innocuous it may seem to be, must be regarded as possibly being a carcinoma. The patient should be admitted to a hospital promptly, all preparations made for a radical mastectomy, and the nature of the lesion proved microscopically. It would appear that we are more in need of education of physicians than of the public in cancer diagnosis. One would like to see the funds recently subscribed by the public for cancer control devoted to providing

graduate training for physicians rather than for propaganda to the public.

Cancer of the breast is one of the types of cancer in which radiation has been extensively tested. About ten years ago we carried out a clinical experiment with radiation in this disease which has given us evidence that has led us to conclusions which are fundamental for us. A series of patients with operable and borderline carcinomas were treated intensively with radiation by Dr. Lenz. The total amount of radiation given to these cases was in general as large as the modern divided dose technique permitted. Several months were required to complete it. After a suitable delay to permit recovery from the acute radiation reaction radical mastectomy was done. In every one of these cases careful microscopical study of the specimen revealed persisting carcinoma cells. These cells usually show signs of having been severely injured by the radiation, and they lie locked up in a dense fibrous stroma. We assume, however, that they are alive and capable of renewed growth. Clinical experience supports this assumption, for we have repeatedly seen carcinomas of the breast that regressed initially following intensive radiation, remained quiescent for two, three, four, or even five years, and then began to grow again. These facts have led us to conclude that radiation will not *cure* carcinoma of the breast, and we have given it up in the disease except as a palliative agent. We do not use it prophylactically as an aid to surgery because operation alone is highly efficient in controlling the local disease, and we have no reason to believe that radiation to the operative field has any effect upon the incidence of distant metastases, our bête noir in breast cancer.

Having been forced by the failure of radiation to rely for *cure* entirely upon radical mastectomy we have attempted to use the operation more critically. Dr. Stout and I have recently worked out criteria of operability. We have found that there are certain types of breast carcinoma that are never cured by surgery. These include the inflammatory type of breast cancer, cases with extensive edema of the skin of the breast, and most cases in which the tumor is solidly fixed to the chest wall. We believe that operation in these cases not only fails to cure but actually shortens life by hastening metastases. In these inoperable cases radiation is the preferred method of treatment, and Dr. Lenz has sometimes succeeded in arresting the disease for as long as five years.

Where breast cancer is operable we believe in performing the

most radical operation that can be done. With modern surgical technique we have been able to extend the original Halsted operation. We remove so much tissue that a large Thiersch graft is required to cover the defect on the chest wall. Our operation requires 5 or 6 hours to carry out, but when done with proper care it has a negligible mortality and it does not cripple the arm. Comparisons in our own hospital indicate that this truly radical operation gives only half as many local recurrences, and a 50 per cent higher five-year cure rate than the usual so-called radical mastectomy. This improvement is no doubt due in part to our more critical selection of cases for operation.

These, we believe, are our best hopes for improving the results with carcinoma of the breast. In younger women sterilization, and in older women the administration of estrogens or androgens, occasionally check the progress of bone metastases temporarily, and in rare cases have been known to retard the advance of the primary tumor. These hormonal agencies, however, are not to be regarded as of much practical importance in the control of breast cancer. Their effects are too inconstant and too feeble to make them rivals of radiotherapy. When they are used as supplements to radiation it is difficult to assess their real value.

Cancer of the Cervix

Carcinoma of the cervix has slightly more than one-half the frequency of breast carcinoma. From the causative standpoint there is one remarkable feature about the disease that gives hope that its incidence can be cut down. This is the fact emphasized by Twombley, that cervix cancer is extraordinarily rare among Jewish women whose husbands have been circumcised. We know also that it is a disease of the under-privileged among whom baths are not in general as available as among the well-to-do. These facts strongly suggest that improved hygiene and a rising standard of living may appreciably reduce the incidence of the disease.

As to diagnosis, we face the problem of educating patients to submit to examination, and of training physicians to do proper vaginal examinations. The disease is often missed simply because examination of the cervix is omitted.

In the overwhelming majority of cases its presence is obvious if the cervix is carefully inspected. A biopsy with a simple biting forceps

suffices to prove the diagnosis. Papanicolaou's method of making the diagnosis from smears may eventually come to be valued as a quick method of singling out suspicious cases for more careful study.

Carcinoma of the cervix is, of course, the one disease in which radiation has become the preferred method of treatment. When used expertly about 35 per cent of five year cures can be obtained with it. The reasons for this comparative success of radiation are obvious. The cervix, being a small hollow organ, can be attacked with radiation both from within and from without. The radiation effect which results is intense, and without doubt completely destroys the carcinoma in many cases.

In keeping with the contemporary general trend toward surgery in the treatment of cancer, the radical surgical attack on carcinoma of the cervix has recently been revived by Meigs in Boston. Taylor and Twombley in our own city have also begun to do the Wertheim operation. They perform it on alternate cases and thus can compare its results with radiation. It is significant of the progress of surgical technique that the lowest mortality that Wertheim himself was able to report in 1911, when he had brought his operation to the peak of perfection for his day, was 15 per cent. Meigs and Taylor and Twombley, however, with our modern technical resources have performed the operation in more than a hundred cases without any operative mortality. The great handicap of the Wertheim operation, of course, is that it can be done only in the comparatively early cases, and these constitute only a limited percentage of all those who come for treatment. It is too soon yet to draw any conclusions as to the usefulness of the operation in comparison with radiation.

We can not leave the subject of cancer of the cervix without mentioning the fact that we owe our modern standards for reporting the results of cancer treatment to the European gynecologists. In 1928, under the Cancer Commission of the League of Nations, they drew up a set of rules specifying the data necessary for statistical purposes in reports of cancer treatment. A special point was that no deductions were to be allowed for patients incompletely treated, for those lost track of after treatment, and for those dying of intercurrent disease within the five year period. If this rule were followed by all who report the results of cancer treatment we would today have a great deal more accurate data for comparison of different therapeutic methods.

Cancer of the Skin

Cancer of the skin is today treated in most clinics with radium or x-rays, under the direction of dermatologists or radiologists. Despite the fact that patients with skin cancer usually come for treatment while the disease is limited in extent, and despite its accessibility, a good many recurrences result following radiation as it is generally employed, and we see all too many tragic cases in which very radical and mutilating surgery has finally to be done. Dr. Stout and I, after seeing the comparative results of surgery and radiation, have come to believe that in most instances it is better to attack the disease surgically in the beginning. Our reasons for this can be summed up under three heads.

1. Surgery incapacitates the patient for a shorter time and is therefore more economical. A surgical wound is healed in a week while a radiation reaction persists for a month.

2. Surgery gives a better cosmetic result than radiation. Scars made with modern surgical technique are almost invisible, while the scar resulting from adequate radiation is a depressed white, telangiectatic, easily traumatized area of skin.

3. Surgery is more certain to cure. With the surgical techniques that the plastic surgeons have developed during the last twenty-five years it is possible to excise comparatively large areas of skin and subjacent tissues and to repair the defect by shifting flaps or transplanting skin. This ability to sacrifice tissues generously gives the surgeon an advantage over the radiotherapeutist, who usually limits his field closely around the lesion. The radiotherapeutist, moreover, is at a great disadvantage where the lesion overlies bone or cartilage, for radiotherapy is not successful with epithelioma involving these structures. Finally, when surgical excision is done it is possible for the surgical pathologist to study the depth and extent of the epithelioma in the specimen, and to give the surgeon an accurate estimate of the thoroughness of removal. The radiotherapeutist lacks any such guide, and his treatment is necessarily less exact and more empirical.

An exception to the assignment of skin cancers to the surgeon should be made for skin cancers occurring in the aged and feeble, in whom radiation is preferable.

Cancer of the Stomach

Cancer of the stomach, the fourth most frequent type of cancer,

is a silent enemy that gives no warning of its presence until it is inoperable in the overwhelming majority of patients. Our problem with the disease is a diagnostic one: gastric resection aiming at cure can be done in only about 15 per cent of those who come for treatment. We must find a better method of detecting its presence in an operable stage if we are to make any headway against it.

Gastroscopy is helpful in some cases, but x-ray study is the most reliable method of diagnosis. Its great disadvantage is its expense. In New York today a gastrointestinal series costs from $60 to $75. Oftentimes patients with vague digestive disturbances, over the age of 50, in whom the presence of the disease should be suspected cannot afford such an expensive diagnostic procedure, and it is omitted.

Many patients with cancer of the stomach have no symptoms at all until the disease reaches the inoperable stage. In an effort to pick up these silent lesions, Dr. Paul Swenson, lately of our Clinic, and now at Jefferson Medical School, studied a series of 2413 patients who had no digestive symptoms of appreciable significance. He made a rapid fluoroscopic examination to determine whether the stomach showed any abnormality, and carried out the usual detailed examination only in patients with abnormalities. Two gastric carcinomas and one lymphosarcoma were found in this manner. Both the carcinomas were early and were resected. This abbreviated type of x-ray examination used by Dr. Swenson would seem to offer the only practical means we have at present of diagnosing gastric cancer at a price within the reach of every man. Although radiologists will protest against using any but the most thorough method of examination, I would answer them by saying that it is better to have used an abbreviated inexpensive method of examination than not to have examined the patient at all. A gastric cancer picked up this way means a life saved.

For we must keep in mind that when the patient's lesion is in an operable stage his chance of cure with present day surgical technique is fairly good. The operative mortality for gastric resection has been brought down from 30 per cent to about 5 per cent during the last generation. The patient surviving resection has at least a 25 per cent chance of five year cure. Recently developed surgical techniques are making possible more and more radical gastric resections and we can hope for some further improvement in the cure rate.

Cancer of the Prostate

Carcinoma of the prostate, sixth in order of frequency, is one of the most formidable enemies of old age in men. From the viewpoint of both diagnosis and treatment our methods are very unsatisfactory, and for the moment there seems to be no immediate prospect of improving them. The radical surgical attack is applicable only to a very small group of cases where the disease is confined within the capsule of the prostate gland, and such cases are rarely diagnosed.

All of us were encouraged a few years ago by the results of orchidectomy and of estrogen treatment. We know now, however, that this therapy is only palliative. It prolongs comfort but it apparently does not prolong life.

Summary

As we have traced the general course of our therapeutic attack on cancer during the last fifty years, and illustrated our theme with examples from the most frequent types of cancer, we see that very real progress has been made in the therapeutic attack. But our curative efforts have been greatly limited and restricted by our lack of good methods of early diagnosis, and our inefficiency in using the methods that we have. For the present our best immediate hope of progress in our attack on cancer is better education of physicians in the use of proved diagnostic methods. This means better undergraduate, as well as more and better post-graduate, education. About two-thirds of the physicians practicing in New York City have no connection with any hospital and they lack therefore the normal educational opportunities that hospital practice brings with it. We must help them, and it is with this purpose in mind that we inaugurate the Academy's Graduate Fortnight in Cancer.

TUMORS OF THE LUNG*

HERBERT C. MAIER

Lenox Hill and Memorial Hospitals

TUMORS of the lung are of great clinical importance because of their frequency and serious significance. With few exceptions primary pulmonary tumors arise from the wall of a bronchus. Whenever the lumen of one of the larger bronchi is encroached upon by a tumor mass, the endobronchial obstruction may result in secondary pulmonary inflammation with pneumonitis, bronchiectasis and abscess formation. Most pulmonary tumors are malignant, but even small benign tumors may prove serious because of secondary infection. Pneumonitis is not infrequently the presenting feature of the clinical picture. Hence the primary underlying tumor may go unrecognized for varying periods of time.

Little can be said concerning the etiology of most pulmonary tumors. The frequency with which malignant tumors develop in an area of chronic pulmonary infection such as bronchiectasis is not sufficient to warrant the assumption of a cause and effect relationship. With respect to the increase in the incidence of carcinoma of the lung, this seems greater than can be accounted for by improved methods of diagnosis. It is possible that the present day heavy cigaret smoking may be related to the prevalence of pulmonary cancer.

Benign Endobronchial Tumors. Benign tumors which arise from the bronchial wall and project into the lumen of the bronchus are rare. Such a benign tumor, derived from one or more of the component tissues of the bronchus, may be a polyp, fibroma, lipoma, chondroma, leiomyoma, osteoma or lymphoma. Adenomas should be considered as a separate group because of their tendency to extrabronchial invasion. The benign endobronchial tumors may cause cough and wheezing but frequently the chief symptoms are due to secondary pulmonary suppuration caused by bronchial obstruction. The diagnosis is established by bronchoscopy and biopsy unless the tumor is in a small branch

* Given at the 19th Graduate Fortnight of The New York Academy of Medicine, October 10, 1946.

bronchus. Endoscopic removal may result in cure if the treatment is instituted before distal suppuration has produced bronchiectasis. Otherwise lobectomy or pneumonectomy is indicated to remove the infected pulmonary tissue.

Malignant Adenoma and Cylindroma. Adenomas of the bronchus have been described under a variety of names, such as benign adenoma, malignant adenoma, mixed tumor of the bronchus, adenocarcinoma, hemangioendothelioma, etc. They constitute less than five per cent of all pulmonary neoplasms but are of considerable importance. The results which may be attained by correct diagnosis and proper treatment are excellent. Adenomas frequently show evidence of local invasion. The regional lymph nodes are occasionally involved by direct extension but only rarely without evidence of direct continuity with the main tumor. Diffuse metastasis from an adenoma of the bronchus which has not undergone obvious malignant change rarely, if ever, occurs. A very few cases with isolated metastases as chance findings at autopsy have been reported. There are a small number of cases on record in which a typical adenoma proven by biopsy was found to have years later the characteristics, both pathologically and clinically, of carcinoma of the lung with metastases. It seems best, therefore, to designate these adenomas as malignant adenomas, recognizing that usually they remain localized and grow slowly over a period of many years, but that occasionally they undergo malignant change and metastasize. The prognosis of malignant adenoma as contrasted with the epidermoid and adenocarcinoma of the lung is so different that failure to consider these two groups separately leads to an inaccurate evaluation of the results of surgical or radiation treatment of carcinoma of the lung.

The term cylindroma has been applied to a tumor which has many of the characteristics of a bronchial adenoma but which, upon microscopic examination, reveals cylinders of cells enclosing either a mucous or hyaline material. Cylindromas of the bronchus not infrequently extend up to the carina or project into the trachea. In approximately one-half of the reported cases the cylindroma either extended to the trachea secondarily or arose from the tracheal wall. Such a finding is far less common with adenomas. Cylindromas also have a greater tendency to local invasion and to metastasis than adenomas. For these reasons they are considered as a separate group of tumors, although in some instances portions of the same tumor may show both adenomatous

and cylindromatous characteristics.

Adenomas and cylindromas occur more frequently in females, in marked contrast to carcinoma of the lung. The majority of cases are encountered between the ages of 20 and 40 years but all age groups may be affected. The symptoms of adenoma and cylindroma may be caused by either the tumor itself or by the secondary suppurative process. Because these tumors are usually located in the larger bronchi, pulmonary suppuration with bronchiectasis and abscess formation occurs in the majority of cases. Empyema occurs occasionally. The symptoms due to the tumor itself are wheezing, hemoptysis and cough. Transient pain is sometimes present even in the absence of infection. When secondary suppuration develops as a result of bronchial obstruction, fever, productive cough, chest pain and other symptoms of pulmonary infection may be present. Some patients give a long history of wheezing and perhaps occasional hemoptysis. In other instances the patient considers himself perfectly well up to the time when a sudden onset of pulmonary infection, often diagnosed as pneumonia, intervenes. Failure of the pneumonic process to clear rapidly under chemotherapy, together with roentgen findings suggestive of chronic pulmonary changes with atelectasis should lead to a consideration of a possible underlying endobronchial tumor. Contrary to the statement usually made in the literature, adenomas may occur in smaller branch bronchi and in such instances may be largely asymptomatic because secondary infection is less common.

The physical findings vary greatly. Examination of the lungs is sometimes negative, but there may be localized wheezing or the physical findings of secondary suppuration and even secondary pleural involvement. Roentgen findings also vary greatly. The roentgenogram of the chest may be negative when there is a small adenoma in the main bronchus, but at this stage a respiratory shift of the mediastinum may sometimes be seen on fluoroscopy indicating partial obstruction to the ventilation of one lung. In some instances, especially if the adenoma arises from a smaller branch bronchus, a circumscribed tumor mass may be seen on the film. In many cases the roentgen findings may be those of secondary suppuration showing varying degrees of collapse of the lung and no direct evidence of the tumor itself. Planography may be of aid in demonstrating the endobronchial obstruction and may indicate the size of the extrabronchial portion of the tumor. Bronchoscopy will

usually establish the diagnosis of bronchial adenoma. The findings at this examination are often rather typical and the diagnosis can usually be confirmed by biopsy. Occasionally the adenoma arises from a branch bronchus not visible bronchoscopically. In such cases the tumor mass is seen on the roentgenogram.

Lobectomy or pneumonectomy is the treatment of choice in those cases of bronchial adenoma and cylindroma in which the patient's general condition is satisfactory. It is my policy at the present time to perform a lobectomy if the tumor can be completely removed by that procedure. Often total pneumonectomy is required because of the location of the growth. If the patient is toxic from secondary suppuration or if pleural complications are present, time should be spent in preparing the patient for radical surgery. Endoscopic removal of portions of the tumor may temporarily produce adequate bronchial drainage with diminution of the pulmonary infection. Because the tumors are vascular there is some danger of hemorrhage during endobronchial manipulation. If the patient's general condition is such as to increase considerably the risk of pulmonary resection, bronchoscopic removal of the endobronchial portion of the tumor may be of considerable benefit. In one of my cases of cylindroma there was a large extension into the trachea which responded temporarily to high voltage radiation. Approximately 90 per cent of my cases of adenoma and cylindroma are living, and all but a few are asymptomatic.

Circumscribed Benign Tumors of the Pulmonary Parenchyma. Included in this group are hamartoma, leiomyoma, lymphocytoma, neurofibroma and plasmocytoma. These tumors, with the execption of hamartomas, are very rare. They are often asymptomatic and may be a chance finding on roentgen examination. The exact diagnosis is established by pathological examination. It is rarely made clinically. Lobectomy is usually indicated. Hamartomas, often called chondromas, consist chiefly of cartilage but also contain cysts lined with bronchial epithelium. A hamartoma is very firm and may thus be confused with carcinoma at operation. Partial lobectomy is usually adequate treatment for a hamartoma.

Angiomas of the lung have been described. Hemoptysis may occur but the lesion may be asymptomatic. When the vascular spaces are large a rather free communication between the pulmonary artery and pulmonary vein may be established. Such cases have been designated

as cavernous hemangiomas or arteriovenous fistula of the lung. A large amount of blood may be shunted through the large vascular channels without the blood being oxygenated. Oxygen unsaturation of the arterial blood results. The patient may present cyanosis, clubbing of the fingers and toes, and polycythemia. A density in continuity with the pulmonary artery is seen on the roentgenogram. Angiocardiogram will confirm the diagnosis. Resection of the involved portion of the lung is indicated.

Carcinoma of the Lung. The clinical picture of carcinoma of the lung varies considerably, depending upon the topographical location of the tumor and its pathologic characteristics. In some cases a large carcinoma in the peripheral portion of the lung is a chance finding on roentgen examination at a time when the patient is asymptomatic and is at maximum weight. A small primary bronchogenic carcinoma may cause few symptoms; the metastatic lesion may be the presenting feature of the clinical picture.

When a bronchogenic carcinoma arises in the main bronchus or near one of the lobar branches, the patient may give a history of chronic cough, later productive of mucoid or blood-streaked sputum and occasional frank bleeding. Many patients, however, never have hemoptysis. There may be symptoms of secondary suppuration. A history of wheezing may often be elicited. Bronchoscopy and biopsy will usually yield a definite diagnosis in this group. When the tumor arises from a smaller branch bronchus in the mid lung field, cough and expectoration may be minimal until the tumor has attained considerable size. If no large bronchus is obstructed by the tumor mass, secondary suppuration may not develop distally, but the tumor itself may undergo central necrosis and liquifaction. When central necrosis of the tumor is marked, the lesion may be misinterpreted as a pulmonary abscess. By roentgenogram the tumor shows a thicker, more irregular wall than is usually found in an ordinary pyogenic abscess. Tumors in the mid-lung field cannot be visualized bronchoscopically, but aspiration biopsy or examination of the sputum or secretions aspirated at the time of bronchoscopy may demonstrate tumor cells.

When a bronchogenic carcinoma arises at the periphery of the lung, there may be little if any cough or expectoration, and blood spitting is usually absent. When such a tumor develops at the apex of the lung, pain in the shoulder region may be the presenting symptom, and the

patient may be erroneously treated for arthritis or other local pathology. An x-ray of the shoulder girdle may demonstrate the lesion in the apex of the lung. Sometimes this lesion is so small that it may be misinterpreted as apical pleural thickening due to old tuberculosis. These patients may have severe pain radiating into the neck and down the arm. Neurological signs, including a Horner's syndrome are present in some cases. When a peripheral carcinoma of the lung extends into the chest wall, a mass, often associated with localized pain, may be the presenting feature. An erroneous diagnosis of tumor or abscess of the chest wall may be made. A primary bronchogenic carcinoma arising in the paramediastinal portion of the lung may closely simulate a primary malignant mediastinal tumor. There may be swelling of the head, neck or upper extremities with venous engorgement, perhaps difficulty in breathing due to extrinsic tracheal or bronchial compression, and occasionally dysphagia from compression and partial invasion of the esophageal wall. Aspiration biopsy, properly performed, is of real value in the diagnosis of the peripherally located pulmonary carcinoma. Many of these lesions are obviously inoperable and exploratory thoracotomy may not be indicated. When a carcinoma of the lung is located near the lower posterior portion of the lower lobe, the symptoms may be referred to the upper abdomen, and upper abdominal pathology suspected. This is particularly true if the chest wall is involved. Occasionally a patient with carcinoma of the lung is suspected of having a primary brain tumor due to cerebral metastasis.

The early diagnosis of carcinoma of the lung is of paramount importance. As already indicated, the history is frequently not characteristic. With early lesions there may be few if any pulmonary symptoms. Hemoptysis is frequently absent. The importance of localized wheezing is not sufficiently stressed. Secondary infection may predominate in the clinical picture. Recurrent pneumonia or a pneumonia which does not respond to chemotherapy may be due to bronchial obstruction by tumor. Early diagnosis of pulmonary carcinoma depends largely on roentgen examination. The appearance of early lesions is frequently not characteristic and may readily be confused with other types of pathology. Any shadow on the roentgenogram which might be a pulmonary neoplasm calls for further investigation immediately.

The value of bronchoscopy in the diagnosis of early carcinoma of the lung has been overemphasized. The statistics from large broncho-

scopic clinics are misleading because the cases referred for endoscopy are obviously selected, and in many instances the neoplasm is seen on bronchoscopy only when the cancer is inoperable. Bronchoscopy establishes the diagnosis early only when the carcinoma arises in the main bronchus, at the orifice of the upper or middle lobe bronchus, or in the larger branches of the lower lobe bronchus. Carcinomas frequently arise more peripherally and therefore are not visible through the bronchoscope when the lesion is small. Aspiration biopsy is another method of diagnosis which deserves wider recognition. Properly performed, the risks and complications are few and the theoretical objections that have been advanced against the method are out-weighed by other considerations. Bronchoscopy, examination of the bronchial secretion or the sputum for tumor cells, and aspiration biopsy all have a place in diagnosis.

Exploratory thoracotomy is recommended in cases of suspected or proven carcinoma of the lung without evident distant metastases and provided the roentgenogram of the chest shows no conclusive evidence of mediastinal invasion. Some patients are rejected for surgery because of their general condition, advanced age and pulmonary emphysema. The most frequent cause for inoperability at the time of exploratory thoracotomy is direct extension of the tumor into the hilar structures.

Pneumonectomy is the treatment of choice in pulmonary carcinoma. Lobectomy is occasionally adequate. Resection of the lung can be performed, however, only in a small percentage of the cases because most patients have advanced disease when first seen by the surgeon. It must be realized that the favorable case of carcinoma of the lung is usually one in which the patient has few symptoms. In the last few years a considerable percentage of the cases that have been most satisfactory for resection have been chance findings on routine roentgen studies. This suggests that routine chest x-rays among the older age group, especially among males, might be a fruitful method of detecting early pulmonary neoplasms. If a lesion is discovered, valuable time should not be lost before initiating adequate therapy. Too often action is deferred in favor of a reëxamination at a later date.

Pneumonectomy is a relatively new operation. To date there have been only a few reports in which the five year arrests following resection for pulmonary cancer have been segregated from more recent cases. Consequently the summaries of some of the reports are mislead-

ing. The survival time following pneumonectomy is greatly influenced by the type of carcinoma resected. Even if malignant adenomas and cylindromas are not included, there is still a considerable variation in the malignant potentialities of different carcinomas of the lung. With few exceptions, our late good results have been observed in those patients in whom the tumor was of the slower growing type. In many clinics about 25 to 40 per cent of the patients in whom a diagnosis of carcinoma of the lung is made are subjected to exploratory thoracotomy. The percentage of the explored cases resected with a hope of cure has varied in different reports from about 25 to 45 per cent. The higher percentages are reported by individual surgeons and apply to selected material and consequently give a false impression of the actual situation in a general hospital. It is obvious, therefore, that pneumonectomy is feasible today in only a small percentage of patients with pulmonary cancer because of late diagnosis. The mortality from total pneumonectomy has decreased markedly in the past few years and is not at present a factor of major importance in large clinics. During the past four years my mortality for pneumonectomy in carcinoma of the lung has been less than five per cent.

There has been much controversy concerning the place of radiation therapy in the management of cancer of the lung. It must be realized that there are a variety of techniques in radiation therapy as there are in surgery. Radiation well localized to the tumor area lessens the unfavorable reaction from radiation pneumonitis. In some selected cases one may obtain real palliation.

Sarcoma of the Lung. Primary sarcoma of the lung is rare. Most of the pulmonary tumors reported as sarcomas several decades ago would be classified today as undifferentiated, small or oat-cell carcinoma. Clinically sarcoma of the lung simulates other pulmonary tumors, especially carcinoma. Occasionally the tumor extends into a bronchus and the diagnosis is established by bronchoscopic biopsy. Errors may occur in differentiating inflammatory tissue and sarcomatous lesions. The treatment of sarcoma of the lung is the same as indicated for carcinoma.

Lymphosarcoma and Hodgkin's Disease. Lymphosarcoma apparently primary in the lung is very rare, but the pulmonary tissue is often involved secondarily in cases of lymphosarcoma. Direct invasion from the mediastinum is frequent. Hodgkin's disease also may involve the pulmonary tissue. Extension through the wall of a bronchus is rare,

but extrinsic compression of the bronchus is not infrequent. Breakdown of the neoplastic tissue with resultant cavitation may occur. Lymphomatoid involvement of the lungs is preferably treated by radiation therapy.

Metastatic Tumors of the Lung. Pulmonary metastases are very common with a wide variety of neoplasms occurring in many primary sites. If the metastases to the lungs are obviously multiple, confusion with a primary carcinoma of the lung is uncommon because bronchogenic carcinoma rarely gives rise to multiple pulmonary metastases. A solitary metastasis in the lung, however, may be indistinguishable clinically from a primary pulmonary tumor. If a thorough clinical and roentgen investigation of other regions of the body fails to demonstrate a primary tumor elsewhere, the pulmonary tumor should be assumed to be primary and treated accordingly.

In rare instances lobectomy may be recommended for a metastatic tumor in the lung. It seems advisable to consider such therapy only if the primary lesion has apparently been eradicated and if the metastatic tumor is a slow-growing, solitary lesion appearing a long time after the primary tumor was removed.

OCCUPATIONAL AND POST-TRAUMATIC CANCER*

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CERTAIN cancers are clearly related to industrial hazard. In the case of still others an industrial etiology has been suggested but proof is lacking and statistical evidence would never pass muster. Among the former are the papillomas and cancers of the bladder, ureter, and renal pelvis resulting from exposure to betanaphthylamine. Not only is clinical evidence clear but abundant experimental proof likewise exists. Others are the skin cancers in workers in paraffin, shale oil, arsenic, tar and pitch, anthracene, the principally scrotal cancers in mule spinners, workers in grease pits, in that vanishing occupation of chimney sweep. Still others are the actinic cancers and when one mentions actinic cancers one does not know where to draw the line of what constitutes industry. The tendency is to think of industrial cancer as mass production cancer yet this is far from a correct view point. The Texas farmer with his keratoses of the hands and face develops industrial cancer. The sailor exposed to sunlight perhaps in the Pacific area during recent years has industrial cancer of the skin and perhaps of the lip. The Egyptian farmer with the schistosomiasis of Lower Egypt, acquired in his fields, and followed so often by bladder cancer, is a victim of industrial cancer. The physician who practises the learned profession of radiology does not like it said that he exercises a trade. Is one therefore permitted to state that the roentgen cancer which he develops through carelessness is an industrial cancer? If this physician develops leukemia, is this industrial? If through roentgen exposure he acquires pernicious anemia, gastric atrophy, gastric polyp, and then gastric cancer, is this an industrial cancer? I believe it is just as were the osteogenic sarcomas in workers in the luminous dial industry during the first world war.

The fisherman who mends his nets with tarred twine which he holds between his lips may get industrial cancer. The glassblower who con-

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stantly inhales hot vapor may have industrial cancer. Certain it is that one will see cases of cancer and of leukemia in our newest group of industrialists, workers in the field of fissionable materials. The ancient Schneeberg-Joachimsthal lung cancer may be due to radioactive inhalations but the matter seems far from settled.

Statements are made to the effect that waiters and bartenders have a high incidence of esophageal cancer. Is this industrial? Do they get them because they drink to excess, are deficient, develop hepatic damage, and if so, shall we call their tumors industrial or cancers due to human weakness? And is the statement even true or does it rest on evidence as filamentous as that which assigns cancer of the nasal cavity to the nickel industry and bronchogenic cancer to the chromium industry?

Casual studies relating cancers to different industries are often casual in the extreme and would not meet the most elementary statistical analyses. In New York I am sure I could show that nasopharyngeal cancer was related to the laundry industry because we see many in Chinese and many Chinese work in laundries. Yet of course the tumor is also high in China and susceptibility to it evidently racial in Chinese. There is a high liver cancer incidence among Bantus and Bantus comprise the labor force in the Rand mines. The tumor has of course nothing to do with mining gold since the high incidence ranges over much of Africa, Malaya, and up the China coast as well.

One must not forget the fact that a cancer may be a highly individual cancer and yet an industrial cancer in the broader sense. Thus a worker will acquire a scrotal cancer if his habits are uncleanly but not if he exercises proper precautions as to cleanliness. If a man is subjected to some unusual incident in the course of industry which results in cancer it would still be an industrial cancer. Thus if a worker in hot metals receives a burn which results in extensive scar tissue formation and through years of breakdown with infection of the scarred area a cancer develops this is an industrial cancer in the broad sense. If a man working in a chemical industry develops a skin hypersensitiveness to a given agent and is treated for his lesions by an enthusiastic radiologist and after years suffers from the results of this enthusiasm one has to admit that the resultant cancer is in a remote sense industrial in origin. One does not think of any cancer hazard in the carpenters' trade, yet anyone with a very large series of cases of lip cancer may find among them the carpenter who for years has held his supply of nails between

his lips. In other words if we view industry in the broadest sense and liberalize our views as to what constitutes industrial cancer we will find not a few cases where individual behavior or individual reactions are directly or indirectly of determining significance.

Intelligent application of gradually acquired knowledge bids fair to eliminate the mass production type of industrial cancer such as betanaphthylamine cancer, but not the individual type. At present mass production cancer accounts for but a minute proportion of the total cancer of any given variety. It is probable that with the development of chemical industry we will see new chemical cancers and medicine must be on the watch for such developments. But it must refrain from hastily ascribing to industry those tumors whose incidence falls well within the expectation for the population as a whole and from making premature conclusions based on lack of appreciation of statistical methods.

Protection in industry can prevent betanaphthylamine cancer. Very large expenditure in the public health field can prevent bilharzia cancer. Industrial lung cancer is probably preventable. Bantu liver cancer may be eventually shown to be dietary and hence be preventable. Thus rather than constituting a permanent hazard in the cancer field the outlook for industrial cancer should be viewed as the most hopeful from the point of view of eventual control.

In discussing the relation between trauma and cancer one must first define trauma as we understand its implication. We mean single uncomplicated trauma. To define this further it is easier to give one or two examples of what is *not* single uncomplicated trauma. For instance, Mr. A. sustains an injury to his femur while at work. He has a compound fracture. After open reduction the healing is complicated and a discharging sinus is present which drains recurrently over a long period of years. The bone, in successive radiographs, shows evidence of an osteomyelitis which does not alter greatly over the years. Then in a relatively brief interval, more than a decade and a half after the fracture, the radiographs show a new process characterized by rather wide bone destruction. At the same time the patient develops some nodes in the corresponding groin area. These when biopsied show squamous carcinoma. The primary site is the intraosseous portion of the old sinus tract. In a broad sense we are dealing with traumatic cancer since had it not have been for the trauma there would have been no suppurating

sinus tract, but in the sense in which we understand single trauma, the case is not one in point.

Mr. B. has a bit of shrapnel in his cheek. It has been there since 1917 or '18. In 1940 or thereabouts he develops deep about the foreign body a low grade squamous cancer. It undoubtedly took origin in epidermis displaced downward by the projectile fragment. The time interval was more than 20 years during which time a foreign body had constantly been present. The trauma is a complicated one.

Mr. C. had a bullet in his hand. It is extracted under x-ray. The time of roentgen exposure used in extraction is said to have been, incredibly enough, 45 minutes. Mr. C. hasn't got cancer yet but most certainly will, but it will be roentgen cancer and not cancer due to the bullet.

A thorough discussion of the relation of cancer to single trauma would require many hours and is obviously impossible in the time allotted. I prefer therefore to discuss single trauma as it pertains to a few varieties of malignant tumors which tend to reach our compensation courts with a fair degree of frequency. Whereas it must be freely admitted that cancers differ in immediate etiology and that argument directed toward the elucidation of one form may by no means apply to another, nevertheless in presenting a thesis in defense of a point of view applying to one specific type, one can develop patterns of reasoning applicable to others. Let us first consider bone sarcoma. I choose bone sarcoma because it is a tumor where many so-called "authorities" would admit traumatic etiology. What do we know about the etiology of bone sarcoma? A certain number arise in long standing osteochondromas, usually central. Another group arises in Paget's disease. A small number have been found in patients suffering from the effects of ingestion of radioactive materials. This etiology has been confirmed also experimentally. A recent report describes multiple origins of osteogenic sarcoma in experimental beryllium poisoning. Another after radioactive strontium and plutonium. Some few have occurred as the consequence of radiation of benign lesions of bone or of "benign" giant cell tumors. I have seen osteogenic sarcoma as the sequence of radiation of retinocytoma in infancy. I have seen two examples of osteogenic sarcoma, one case multiple, arising in Gaucher's disease of bone and several in fibrous dysplasia. This leaves a large number of primary malignant bone tumors unaccounted for and at present we have no explanation of their existence. This fact however does not mean that we must look for

such explanation in trauma.

The sincere investigator works under great disadvantage when he endeavors to elucidate the role of trauma. Hospital histories usually taken by residents are of essentially no value. Statements of patients are accepted as bona fide and go down in histories without critical analysis and without the slightest evidence of skepticism. When a case reaches a compensation court the claimant's testimony is of no scientific value whatever despite what a referee may think. The stories told may combine the best features of Baron Munchausen and Alice in Wonderland.

Unfortunately I do not believe that medical testimony of the average sort is much better. First of all the physician unfortunately is testifying for a fee or in order to collect a bill for services rendered and I am sufficiently skeptical of my colleagues to believe that some, at least, share the common herd's instinct to collect where they can. I feel therefore that any case of medicolegal import is prima facie one where an attempt at scientific evaluation is apt to yield material of very doubtful significance. This at once restricts material to be analyzed to cases with no medicolegal import. Now it would seem that they might afford an answer but they do not. They do not because the average surgeon does not know how to question a patient. If I had my way I would turn over every such case claiming trauma to a psychiatrist to see how an original story of trauma would end up. I have reason to believe that the end story might be far different from the original.

We might ask ourselves what accessory evidence can be brought to bear concerning traumatic etiology of bone sarcoma. I believe the accessory evidence of negative character greatly outweighs the supposedly direct evidence of positive character. Thus: the supposedly precipitating trauma is usually mild or even minimal. In a previous lecture on this subject I have called attention to the fact that I personally had seen no osteogenic sarcoma following the maximum trauma of fracture. Since then I have seen one possible one although I regard the prior integrity of the bone as doubtful. Statistics are hazardous things. I am however informed that perhaps once in ten years in New York State an osteogenic sarcoma within a year of fracture might occur in a given bone on the basis of chance alone without etiologic relationship. It so happens that I see a large number of the osteogenics originating in this State—what exact proportion I cannot say—and that I have had one such case in 18 years. I make no claim for the validity of the statistics and as

stated above am by no means sure of the primary integrity of the part in the instance concerned. Be that as it may it is still a fact that the severest trauma to bone, namely fracture, is the least apt to yield sarcoma. Further accessory evidence of negative character comes from surgery. Surgery involves screws and ice tongs, removal of wedges for correction of deformities, resections with insertion of grafts, highly traumatizing spine fusions, and yet no sarcomas seem to result. The highly disruptive lesions of Charcot joint or syringomyelia produce no cancers. The multiple infarcts of caisson disease seem to "heal" without event. If subperiosteal hemorrhage causes regenerative changes leading to sarcoma why do we not hear of it from the hemorrhages of scurvy? The prolonged inflammatory changes in bone resulting from osteomyelitis do not result in tumors. When sinus tracts lead down to bone and one has excavations with prolonged suppuration the cancer which develops is always squamous carcinoma and never osteogenic sarcoma. One of the most traumatizing procedures to bone is found in one of the commonest operative procedures on man, namely exodontia, and whereas osteogenic sarcoma leads to exodontia under mistaken diagnosis, the reverse never seems true. The proliferative periosteal changes which accompany other tumors, of which the most striking example is meningioma, although they may exist over a period of many years do not result in the conversion of the process to osteogenic sarcoma. Thousands of amputations have been performed since the early days of surgery and although one saws through bone, regularly elevates periosteum, possibly uses forceps or rongeurs to improve the appearance of the stump, we do not see any rapidly developing fungating sarcomas as sequelae.

How common are malignant bone tumors unsuspected by the patient? We naturally cannot say. I have seen them. I had a couple of years ago an unsuspected malignant bone tumor of a rib discovered in a draft board examination. Dr. Jaffe informed me a few months ago that he had found a very early osteogenic sarcoma in a patient who had a film taken immediately after a bona fide trauma. Had that film not been taken the case would have in all probability fulfilled the criteria for traumatic osteogenic sarcoma. It is certain that a number of chondromas are encountered as incidents of radiographic study for other conditions, and that chondromas constitute foci for later development of sarcomas.

One derives the impression that malignant bone tumors have rather highly specific causes which so far remain unelucidated. Specificity for

example appears in the high incidence of osteogenic sarcoma in Paget's disease and the essentially zero incidence in generalized osteitis fibrosa cystica. It may also appear in the case of the solitary central chondroma as a source of sarcoma on the one hand, and the lack of evidence on the other of sarcomatous tendency in the case of the epiphyseal chondroblastic tumor described by Codman. Proponents of the theory that post-traumatic regeneration of bone is of causal significance in development of sarcoma should be exposed to the histologic appearance of normal bone growth at epiphyseal lines where absorption and growth are coincident phenomena over the entire life period of bone growth. True it is that these zones are likewise the common site for osteogenic sarcoma but if post-traumatic regeneration causes the majority of bone sarcomas then I cannot see why most people with normal bone growth don't develop this disease since all of us exhibit essentially the same regenerative phenomena without any trauma.

In emphasizing normal processes in tissues or organs which duplicate exactly effects ascribable to trauma I like to use one very pertinent example. This is the uterus. One does not hear of uterine cancer being ascribed to trauma yet there is in existence plenty of testimony to the effect that cancer of other mucosal-lined viscera may be so ascribed. The facts are, of course, that the uterus of the normal female traumatizes itself physiologically every 28 days from about the age of 14 to 15 in these climes to that of 45 to 50 or upward. The average female sustains some 400 traumas all accompanied by hemorrhage, slough, and very active regeneration. The average female who gets a carcinoma of the endometrium does so some years after all trauma has ceased. Similarly the ovary traumatizes itself once a month yet no one considers an ovarian carcinoma traumatic.

The normal wear and tear of life induces a multiplicity of traumas which are rarely noted or quickly forgotten until the time arises to make something out of them. I strongly advise the advocates of the traumatic etiology of cancer to take a few hours off from their deliberations and concentrate upon observing a group of children at play. They will, I can assure them, in the course of an afternoon witness all the types of injury supposed to cause cancer and unless hard-hearted will return home greatly depressed at the sad outlook for the future these children possess.

Advocates of the role of trauma rarely if ever consider a role for in-

fection in the genesis of cancer. I would think that if trauma possesses a role, then infection should possess an even greater one, for the tissue changes of infection would seem to resemble although in more severe form those of trauma. In infection tissues die, exudates accumulate, vascularizations occur, scar tissue results, and parenchymatous tissues are stimulated into regenerative growth. Yet the individual who testifies that a bone sarcoma has arisen because of trauma would not worry about a case of osteomyelitis eventuating into osteogenic sarcoma. He does not think that a breast abscess will become a breast cancer, a lobar pneumonia a bronchogenic cancer, an amebic abscess of the liver a hepatoma, a carbuncle a liposarcoma, a psoas abscess a myosarcoma. He has never professed an opinion that the proliferated nuclei in widely disseminated foci in that very common disease trichiniasis form the starting point of muscle sarcoma. For the most part these things have never entered his head because he has promptly forgotten his pathology after the end of his sophomore year in medical school.

But be that as it may, we have gotten away from bone tumors. Some years ago I formulated a brief statement in the course of talks to medical students. Facetiously I called it Stewart's Law and it goes like this: The probability that a given lesion is a primary bone sarcoma, all facts being correctly stated, is inversely proportional to the degree of trauma sustained. This statement has been improved by my associate, Dr. Foote and might read "To establish the traumatic origin of tumors requires that one be able to prove that trifling injuries are vastly more cancerigenic than are major injuries."

Mammary cancer appears with fair frequency in our compensation courts. It is a common disease and the minds of many women have been through generations impressed with the fallacy that breast cancer follows a blow. Surgeons and to a lesser extent pathologists are misled by careless statements in books and fail to reason on the basis of facts which of course they may not even know. Now mammary cancer in the human subject is largely a disease of mammary ducts. It has been said that traumatic mammary cancer may follow the "rupture" of ducts but the trouble is that no one sees "rupture" of ducts until the cancer is already lining these ducts. The commonest cause of severance of mammary ducts is surgery performed for benign lesions of the breast. If this is the commonest cause of breast trauma then it should be the commonest factor in etiology of cancer. Some support might be supposedly derived

from statements to the effect that patients operated on for benign lesions –notably the various manifestations of cystic mastopathia–have a higher than expected incidence of subsequent mammary cancer. This is true *but* the difficulty is that the higher incidence may be in *either* breast, the operated one or the intact one. This of course negatives the influence of trauma in the causation of breast cancer and throws the emphasis to the field of cystic-proliferative lesions of the breast whose influence is in turn most difficult to ascertain through actual statistical study although few with large experience could question its participation. Most surgeons fail to appreciate the fact that when they see a mammary cancer which they can feel it has been there a long time and has been preceded by a progressive transformation of a region or regions of the duct system leading to the development of a carcinoma in situ. It is impossible to say just how long this phase lasts but if we judge from evidences presented in those fields where chronology is somewhat known we might extend the in situ period for several years, perhaps five and maybe more. Furthermore, cancer of the breast is a system disease, often bilateral, and successive segments of the mammary apparatus are involved first by an in situ and later by an infiltrative type of lesion as the attribute of malignancy in the cancer cell becomes more and more manifested. The acme of change is reached in the extensive bilateral type of disease. I would refuse to entertain even the suspicion that mammary cancer is caused by trauma. One of the most convincing cases for traumatic etiology is that reported by Rixford and seen and partially accepted by Ewing. We might ask how the evidence stacks up. The patient was a boy of about 17. He struck the right breast and sustained a verified trauma. The breast swelled to large size. Treated conservatively the swelling diminished and 6 months later a rather small flat discoid lesion persisted below the nipple. A surgeon locally excised it and threw the tissue away stating that it was like other gynecomastias which he had seen. No tumor subsequently appeared in this breast and in fact the next *external* evidence of disease was found in the *opposite* axilla. The patient later died with widely disseminated lymphatic permeation and metastases in the neck, both axillae, mediastinum, mesentery, about the prostate, in the skin of the trunk, and in fact "everywhere except in the skin and subcutaneous tissues of the right breast, the site of the surgical operation." Parenchymatous metastases were rather rare. No primary tumor was found at autopsy. I have seen these sections and to

me the lesion looks more like a gastrointestinal than like a breast cancer since the cells possess mucus droplets and a trace of signet ring structure. Growth too is more papillary than is to be expected in disseminated breast cancer. Neither the age of the patient, the sex, nor the distribution of disease fits the story of breast cancer. The fact that no primary was found does not impress me because I have myself failed to find primary tumors occasionally and recall one case seen by the late F. B. Mallory where an insignificant primary was nearly missed and was in fact only discovered after the body had been reopened and a tiny lesion of the ampulla of Vater detected. All sorts of traumatic incidents are described by claimants seeking compensation for breast cancer. They range from the sublime to the ridiculous. I recall one case where a lady fell on her back and pressed a small drinking cup to her capacious bosom and this incident had to go through the usual routine of the compensation board. I recall another, not of medicolegal import, where a lady had attended the funeral ceremonies of a friend who had unfortunately died of breast cancer. She was greatly worried and immediately examined her own breasts and found a lump which proved to be cancer. Perhaps that is a case of acute psychic trauma. One can almost see the frenzied activities of the neural mechanism on the way back from the cemetery, the acme of psychosomatic medicine.

The earlier one sees mammary cancer the less one is apt to see any suggestion that an episode has occurred in the surrounding tissues which could have been produced by trauma. One does not see evidence of old hemorrhage. One does not see undue fibrosis save in the breasts which are already extensively fibrosed and atrophied. One does not see the cancer within the ducts accompanied by inflammation except as a *result* of the cancer and in fact the striking pattern in the earliest phase of breast cancer within ducts or their terminal lobules is the utter lack of anything abnormal whatever besides the cancer except in some instances its predecessor, the papillary hyperplasias. Everywhere one gets the impression that the cancer process is something intrinsic within the cell of origin uninfluenced by external or for that matter internal factors which show themselves through perceptible alterations in surrounding tissues. Here and there a few cells are cancerized and if one wished to invoke trauma in explanation the trauma would almost have to be induced by use of something like a Chambers micromanipulator.

Whereas a survey of older textbooks particularly of surgery pro-

duces numerous statements to the effect that breast cancer may be traumatic they belong for the most part to the category of books which state that breast cancer *follows* eczema of the nipple and the two statements are of equal validity, showing equal pathologic knowledge. Late publications issued by anti-cancer organizations such as that in Massachusetts tend to deny these obsolete theories. One only, issued in Minnesota, is unwilling to deny the traumatic etiology. I suggest that this represents someone's personal idea since *only breast cancer* is mentioned as possibly traumatic, and no others. It is strange that it would assume this unique position.

A third group of tumors commonly ascribed to trauma are tumors of the testis. The fact that an identical type of tumor, which without statement as to location could not be distinguished microscopically from these testis tumors, happens to occur in the ovary where surgeons do not incriminate trauma, attracts little comment. Strangely enough, too, they occur in the pineal gland. In the ovary they are known in the preovulatory age group and hence "normal" traumatic incidents cannot be invoked in explanation. Likewise the fact that testis tumors occur in abdominal testes where the organ is far removed from trauma is strong evidence against the traumatic hypothesis. There is considerable evidence to incriminate developmental disturbance of unknown origin as a factor in production of testis tumors. Thus although pseudohermaphroditism is not a common state it accounts for about 1 per cent of testis tumors and in these cases as reviewed by Gilbert who analyzed some sixty, forty-eight were in abdominal testes, eight in inguinal testes and but two in a scrotal testis. Eight were bilateral.

Concomitant ectopy occurs in 11 per cent of testis tumors, or forty-eight times the chance association and in unilateral ectopy the tumor is in the ectopic organ in 97.5 per cent of all cases. When a testis tumor occurs in a "normal" testis the chance of its being bilateral is but 1 per cent but when bilateral ectopy is present the chance of bilaterality of tumor rises to 11 per cent. Wells reports seminoma associated with complete failure in development of the right genital anlage and immaturity of the left anlage. On the other hand there is no suggestion that the incidence of malignant testis tumors is increased by the trauma concerned in orchidopexy and the interval between surgery and tumor ranges from 5 to 12 years in teratoid and unicellular types respectively.

A testis may be the site of unsuspected tumor. This has repeatedly

been shown in instances where the first suggestion of disease appeared from distant metastases and the primary tumor was only demonstrated by careful autopsy study. I have seen testis tumor in supposedly non-neoplastic ectopic organs removed at herniorrhaphy and one in a testis removed immediately after a severe scrotal trauma where crushing of the testis was present. The latter would have constituted a perfect case for trauma had the testis not been removed in a matter of hours.

That tumors occur in supposedly normal testes has received confirmation from veterinary studies. A fairly recent report disclosed three unsuspected testicular tumors of horses in the course of 250 gelding operations. The various inflammatory lesions affecting the testis, although so far as tissue changes are concerned these lesions should count as a histologic equivalent of trauma, do not seem to influence the incidence of tumor. Thus in 5500 testis tumor records Gilbert found records of orchitis due to mumps in but twenty-four and an average interval between orchitis and tumor of 12 years—just about the difference between the average age incidence of the two diseases.

I have heard the statement made that in 30 per cent of testis tumors the disease is due to trauma. One immediately asks what causes the other 70 per cent. To make such a statement is to my mind the equivalent of saying that 70 per cent of cases of smallpox are caused by a filtrable virus but the other 30 per cent are caused by trauma. The fallacious approach is very obvious and were one to think back over decades and centuries there is scarcely a disease to which this form of false logic could not be applied, for in the infancy of medicine etiologies were wholly obscure and had there not been available a host of malign influences and a vast source of magic, undoubtedly trauma would have played a much greater role than it ever did, in the field of disease in general. In my own early days I learned on local medical authority that a certain child in the neighborhood had acquired paralysis, clearly poliomyelitis, because the nurse had dropped him. Why an identical twin had gotten it within hours thereafter was not explained.

As one author succinctly expresses himself "Because toads appear after a rain it is not necessary to assume that it has rained toads," yet this form of reasoning fills our medical testimony concerning trauma.

Advocates of the traumatic etiology of cancer, aware of the difficulties which underlie their suppositions, may take some refuge in the thesis that the individual who suffers from what they term a

traumatic cancer is one who possesses what they call a predispositon. They do not define predisposition but I understand the term in two different senses. First it might mean a hereditary reaction pattern to the injury sustained and I would widen their use of this definition to state that without hereditary reaction pattern in its broad sense no tumor can occur and that the function of biology is to determine these reaction patterns and the factors of realization which bring them into evidence. Secondly they may mean that a set of conditions, perhaps the existence of something in the nature of a virus or chemical agent, may already obtain in the injured area which agent may give rise to tumor when the soil is suitably traumatized. Some take refuge in the essentially obsolete Cohnheim theory of surplus cells which are thought of as only awaiting a suitable trauma to goad them into action. Unfortunately no one has seen these cells. What is curious about the thesis of predisposition as commonly maintained is that its proponents neglect the temporal factor. Evidently it is only at one time when the malign influence of trauma can give rise to cancer. The part injured may have been injured almost ad lib at other times and nothing unusual happens, or it may be that injuries to other constituents of a system, muscles, bones, or soft tissues occur at the same time but only in the temporarily predisposed part does tumor arise. The great difficulty is that human medicine has no method of answer to such suppositions and hence cannot deny them and unfortunately they are not subject to experimental proof or to complete rejection on logical grounds. One cannot argue without fact.

I have emphasized the unreliability of hospital charts relating to injury. I could give illustration after illustration to support this conclusion. Statements by patients may be deliberate falsification but are often unconscious misstatements. I could cite you the case of a man with a bulky basal cell tumor of the skin of the temple which was related to a blow from an iron bar through many medicolegal squabbles but which was admitted to have long antedated that alleged injury after the claimant had become slightly enamoured of a social worker to whom he confessed. Within the last few months I had an accidental example of the inadequacies of history taking in the shape of a story told by an employee of my own apartment. The story did not involve compensation. The patient had an extremely advanced tongue cancer which he related to injury from a fish bone. That he had stuck himself with the bone was beyond shadow of doubt because he was so impressed by the injury

that he kept the bone wrapped in a bit of paper in order to exhibit it to on-lookers. Still he had stuck himself twice with the same bone and the tumor was well back in the tongue which made me suspect that an organ twice severely traumatized could scarcely have been of normal motility or sensitivity. I questioned the man myself and he denied any evidence of prior disease until I was about to give up the inquiry whereupon he added as an innocent afterthought the statement that there was "nothing except that when I smoked a cigarette it burned me back there. When I stuck myself it bled and bled and bled." One does not forget that in giving the findings when a small biopsy is secured from an open lesion one of the commonest statements one sees on a history sheet is "lesion bleeds easily."

I will never forget a curious example of the casual in history taking in a case in the Memorial Hospital where the chart states that the patient had been bitten by a duck. This statement persisted for years and excited no curiosity until viewed by a resident who knew something about ducks. He asked the patient what sort of duck had bitten him wherupon the patient responded "It vos a bool duk."

About two years ago a certain letter appeared in the Journal of the American Medical Association. It was apparently written in rebuttal of one written by me in which I called attention to the credulity of physicians and courts in the acceptance of the doctrine of single injury as a cause of cancer. The writer obviously considered that his rebuttal was just and complete. He dealt with facts as he had them, or rather *hadn't* them, and I hope to use this particular proceeding in order to show what cannot be accepted in evidence. First I quote portions of the published letter: "In April 1935 about 11 P. M. in S———, Kansas, P———, in the course of his employment, was carrying a box of books. He stumbled, the box struck and damaged the top of a desk and P's chest struck the box. Before quitting work about 1 A. M. P——— left a note for his supervisor reporting the accident. Whether or not he reported that he had been hurt is unclear but when he reached home he told his wife of the accident, and that his chest had struck the box and was hurting. There was no evidence up to that time that he had suffered any chest pain. His wife did not examine the chest until 3 or 4 weeks later. Then she found a red spot. A month to 6 weeks, possibly 2 months after the accident he told his supervisor that he had hurt his chest when he fell with the box of books and that the lump on his chest was caused

by the bump or bruise." Then the writer of the letter asks the following evidently rhetorical question: "Was not the injury described the exciting cause of the sarcoma that followed. Before denying a causative relation one should point out some reasonably likely cause other than the injury. Before attributing the entire incident to the so-called laws of chance one should consider the incidence rates of sarcomas of the sternum and of contusions of the sternum on the entire population and then estimate the chances of such contusion and such a sarcoma coincidently in site and in immediate chronological sequence."

Now to me this sounded like a striking case and evidently the courts thought so too for they awarded full compensation. But it sounded too good and I wrote for copies of the testimony and reviewed the situation at length. After this review I can honestly say I have never seen a more extraordinary situation. Let us briefly review the facts apparent in testimony. The claimant was the patient's wife, the patient having died. Hence most evidence was hearsay. The patient was a janitor. He did mar a desk. He reported this by leaving a note for his superior. The latter destroyed the note. He testified that he recalled the note stating that damage had occurred to a desk but recalled nothing about the patient stating that he had hurt himself. But the commissioner ordered stricken out the last part of this testimony about the patient not having stated that he injured himself thus concealing what to an unprejudiced person is important. Still perhaps that is correct procedure for later on the fact is brought out by direct questioning. Then it appears that the wife's testimony is accepted as bona fide. She testifies that when the patient came home "he said that his chest was hurting him awful bad." She does not state that the husband told her he had reported an injury to his chest but believed so. Despite the fact that the patient's chest was hurting him very badly this loving partner did not see fit to examine the allegedly injured part and only did so some weeks afterward. Incidentally even the date of this injury appears uncertain. It might have been in February, March or early April. It would seem to me that a bona fide injury might have been more definitely placed in time.

Now later on it appears that the patient was told by the doctor that his lump was due to an injury. The alleged relationship was something stimulated by a physician looking for a cause for something he didn't understand. One wonders if the patient were not more astute than the doctor because the former never filed any claim for compensation during

his lifetime and the institution of claim seems to parallel roughly the receipt of bills for medical and funeral expenses.

Nowhere in the testimony does it appear that first appearance of tumor and site of alleged injury corresponded. To cap the climax there is not a shadow of evidence that the man had a sarcoma at all for the material removed at surgery was thrown into the bucket without pathological examination.

Have we any right to assume that the fact that the operator made a diagnosis of sarcoma proves it to have been? I could not myself from gross examination alone and the very fact that this patient was seen by physicians for a period of 13 months prior to operative interference does not convince me that diagnostic acumen in S———, Kansas is on a higher level than that in New York. Then I am interested in the radiographic findings. The tumor was destructive, destroying sternum and rib cartilages. This sounds to me like a metastatic carcinoma and from my past experience with sternal tumors I would hazard a substantial bet that Mr. P——— had either a penetrating lung carcinoma or a metastatic renal cancer. It is interesting to note that his physician had for some time prior to the alleged accident been treating him for "bronchial trouble."

I believe the rhetorical question posed in the Journal of the American Medical Association is fully answered. I cite this case as an almost perfect example of the hopeless character of analyses we find in many cases where questions of traumatic etiology of cancers are raised.

It must be quite obvious that none of the postulates, in which the medicolegal expert has for years taken refuge in acceptance or non-acceptance of a given case as traumatic, are fulfilled in the latter case. I do not propose to discuss these postulates save to say that they are only exceedingly rarely fulfilled in any case of traumatic cancer so-called. In fact it is in many instances frankly impossible that they can be fulfilled. I do however wish to call attention to the fact that, when in the rare case they are, it really means nothing at all and the reasoning involved in acceptance of a traumatic etiology of a cancer is still of post hoc ergo propter hoc type and as science it has no value whatever. We still do not know what causes the tumor and our reactions are conditioned upon emotional rather than scientific grounds. Let us not forget however that we do have a very ready source of material for study where all the necessary postulates demanded by the medicolegal expert

are at hand, prior integrity of the part, exact extent of injury, specific tissues injured, exact site traumatized, known time factors and everything. That source we have mentioned in passing but should now emphasize in concluding and the source I refer to is surgery. More tissue damage is done by surgery than by any other form of injury and I have yet to meet the surgeon who can recall the fact that his years of activity have produced a single tumor, other of course than a simple keloid which never becomes malignant, or an amputation neuroma, likewise benign. It is doubtful if either of these lesions should be dignified with the name of neoplasia.

I have said nothing about the role of trauma in accentuation. To discuss this would require considerable time. Accentuation has to be evaluated on the basis of knowledge of natural history of the disease in question. It is not enough to accept accentuation as a fact in the case of an individual who has sustained a trauma to a tumor and has thereafter experienced what may be supposed to be unusual growth activity on the part of the tumor. The change in behavior must be something praeter naturam, beyond "nature." As one's experience in the spontaneous behavior of neoplastic diseases increases the fewer will be these unnatural alterations in behavior until they almost approach a vanishing point. Let me cite two examples to illustrate our difficulty: Mr. A. has a tumor of the upper end of the humerus. The periosteum is elevated but intact and growth is proceeding under the restraint of a tense capsule. A surgeon cuts down on the lesion, enters the periosteum, secures a specimen, does not close periosteum or the tissues in layers but instead leaves in a drain. The tumor rapidly fungates. This is accentuation. The tumor may in a matter of two or three weeks become inoperable. On the other hand Mr. B. has had a rib tumor for 5 months at least. On July 5th this rib and the two adjacent ones are resected down to and including parietal pleura. The chest is open and careful inspection reveals one tiny pinhead size nodule on the diaphragmatic pleura. This is tumor. Nothing else is seen. A nodule is felt in the underlying lung which is decorticated. This nodule is a Ghon tubercle. The convalescence is uneventful. The tumor itself has not been touched. The patient is discharged on the 11th day feeling well. About three weeks thereafter he suddenly feels weak, becomes dyspneic, and has a temperature. He re-enters the hospital where it is thought that he has a late postoperative effusion. He is tapped and only blood is obtained. He

dies less than two weeks later and at autopsy the pleura, previously clear, is overgrown on all its aspects, from base to apex and from parietal to mediastinal, with a sheet of tumor two inches thick and both lungs, clear five weeks previously, are riddled with tremendous metastases. I stated that the first example represented traumatic accentuation. After the second where tumor was not touched, we must ask ourselves, does it?

In conclusion were I required to state my position on the relation of single trauma to cause of cancer I would state it briefly as follows:

Attempts to rely on single trauma to explain cancer depend on the exercise of primitive forms of reasoning.

They represent a carry-over from pre-pathologic days and appear in textbooks which copy from one another and are repeated by writers who do not think or who lack the wherewithal to form judgment.

They are propagated by a system of compensation medicine which denies payment for services to a physician who may in good faith have assumed care of a patient, unless that physician shall prove a traumatic etiology for the disease, and since the physician is human and can find plenty of so-called authorities to support such etiology he is very apt to endeavor to prove it, although I would warrant that for the most part he does not believe it himself.

They are likewise propagated by patients who lack information on origins and natures of disease and who for years may have been conditioned to relate lumps and therefore cancers to blows. Such patients readily fall into faulty logic especially with lay, medical, and, above all, legal aid.

They constitute a small but steadily increasing problem in sociology which I do not pretend to be able to solve.

SKIN TUMORS*

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DISASTROUS results from cancer of the skin are in almost all cases avoidable by removing the irritants known to influence the development of cancers, and by thorough treatment of pre-cancerous and cancerous lesions.

Skin cancers in their incipiency and throughout their entire course are interesting in that they are an open book, so to speak, that he who will—and can—may read.

As you know, there are three main types of skin cancers: The basal cell epithelioma (benign, non-metastasizing); the squamous cell epithelioma (metastasizing); the malignant mole or melano-carcinoma.

Basal cell variety: There are a number of different types, the most important being the rodent ulcer, the morphea type and the multiple benign superficial basal cell epithelioma. The particular variety of basal cell epithelioma probably depends upon its location, the carcinogenic factor and the tissue from which it originates. Rarely are there symptoms connected with the two latter varieties of superficial growths, except that occasionally one may ulcerate, simulating Bowen's disease (dyskeratosis). While each of the basal cell types may differ from the others in appearance and in the degree of local destruction, all have certain features in common, the outstanding one being the pearly or waxy telangiectatic margin or rim. They are slow growing, cause only local destruction and probably never metastasize. Metastasis is so rare that when it is observed, one must question the correctness of the diagnosis on the original tumor.

The rodent variety is usually the most destructive of the group, and over several years' period may cover a wide area and cause considerable destruction, especially where an irreplaceable part is involved, such as the eyelids or nose. Such ulcerations sometimes have to be differentiated from the gumma of syphilis, tuberculosis and blastomycosis, though usually the history of several years' duration, the waxy or pearly nodu-

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lar border, the crusted and red, bleeding granular base, serve to identify the epithelioma. The duration of lupus is usually longer than epithelioma. Biopsy should make the diagnosis conclusive.

I have seen recently three cases of gumma which had been diagnosed and treated by radiation for carcinoma, the treatment being followed by a severe reaction, including redness, swelling and sloughing of the parts. Gummas are apt to be found on an extensor surface at the site of trauma. They develop rapidly, usually are kidney-shaped, with deep, punched-out bases and bevelled, soft edges. The Wassermann is almost always positive.

Tubercular ulcers usually are distinguishable from carcinoma by their ragged, undermined verrucous edges, and by the tendency to heal with scar formation and, oftentimes, with recurrence of tubercular lesions within the scarred area.

Blastomycosis is a warty, crusted lesion with multiple discharging sinuses. The fungus can most often be demonstrated.

The morphea variety, as the name implies, often strikingly resembles scleroderma. The lesions may vary from pea-size to that of a man's hand and be shiny, smooth, the color of yellow wax, and have a slightly raised telangiectatic margin. These lesions never ulcerate and, except for appearance, cause little or no inconvenience.

The multiple superficial basal cell epithelioma, contrary to most of the benign types, which usually appear on exposed parts (chiefly the face) is found on the covered areas, often the trunk, arms and thighs. These lesions vary in number from one to a hundred or more, and in size from a small pea to—in exceptional cases—that of one's hand. They are deep red, scaly, with scarring in the center and with a threadlike characteristic pearly border. These growths are sometimes mistaken for and treated as psoriasis—as was a case which came under my observation a few weeks ago. This patient was suffering from an active pulmonary tuberculosis, and inasmuch as there had been no response after a year's treatment for psoriasis, the physician who had sent him to me thought that the skin lesion might be tubercular.

Most of the patients with the superficial basal cell epitheliomas have been under treatment with arsenic in earlier years, and it is now believed by many physicians that this drug may be responsible for the growths. Indeed, in many instances, arsenic in excess may be demonstrated in the blood and urine of such patients.

Squamous cell carcinoma (the metastasizing variety), while relatively benign and usually accessible to removal may, if neglected, or mistreated, spread to the internal organs and cause death. These growths may occur on any part of the cutaneous surface, but they are more often found on the extremities and uncovered parts, and at the site of some long-standing irritations, such as x-ray burns, scars, chronic ulcerating skin diseases, in arsenical keratoses, in cutaneous horns, in xeroderma pigmentosa. All tumors beginning on mucous membranes are of the squamous cell variety.

Characteristics of this sort of tumor are: its comparatively rapid growth, an accompanying inflammation in and around the lesion, the verrucous ulcerating and sloughing base, and the hard nodular borders. Some early and atypical lesions cannot be distinguished from basal cell epithelioma without a biopsy. While it is generally thought that most carcinomas that form in an x-ray burn are of the squamous cell variety, it interested me to find that under biopsy study of the last eleven such growths I have removed, eight proved to be basal cell epithelioma, two squamous and one baso-squamous.

I believe it imperative that one take a biopsy, either before or at the time of treatment of every epithelioma; not only is such laboratory information of diagnostic value, but often one can determine the depth and the degree of malignancy. It would seem that whether a given skin tumor proved to be of the basal cell or squamous variety, might depend on the location, the duration and the degree of irritation.

Melano-carcinomas, the third group, are by far the most malignant of all skin tumors, though the degree of malignancy may vary considerably in different individuals, according to the age of the patient, the location of the primary lesion and the type of tissue from which it originates. For example, a melanotic nodule appearing on the cutaneous surface of an adult may cause metastasis and death in a few months, while a similar growth on a child may require many years to cause death.

I have in mind three cases in which melanotic growths were removed from the eyes of children—and in one of the cases, a few months later a similar melanoma from the forehead. The diagnosis was in each case confirmed by a pathological report, yet these patients after 20-26 years are still well. The prognosis in cases of melano-carcinoma arising in the skin is also much more favorable in children.

Melanoma is first noticed as a pinhead to a pea-sized, bluish or brownish-black papule, more often on the sole of the foot, around a toe or finger nail, on the buttocks or on the forearm. The lesion increases gradually so that in six months or a year it may be the size of a hazelnut, with bluish lines radiating from the tumor. At this time the regional glands may or may not be enlarged. Then pea or almond-sized nodules may appear beneath the skin near the original lesion and spread gradually over all the cutaneous surface; the glands, liver and the spleen become enlarged. Melanine is found in the urine. Sometimes these melanotic growths originate from moles which have been subjected to frequent irritation or that have been incompletely removed. Such tumors are highly malignant and usually terminate fatally.

Melanoma must be distinguished often from blue nevi, fibro-angioma, epidermal nevi, pigmented basal cell epithelioma and from pigmented moles. Blue nevi have usually been present and unchanged since childhood, or for many years, and are dark blue to black in color and sharply circumscribed. Rarely does one become malignant, and if it does, it is usually a melano-sarcoma.

Fibro-angiomas are most often on the face, and are hard, lobulated, blue in color, and have usually been present for a year or more without noticeable change. Epidermal nevi may be from pinhead to pea-sized, macular, tan to dark brown in color. The pigmented basal cell epithelioma may be recognized by the history of a keratosis of several years' duration, and the verrucous, ulcerated character of the lesion, and the pearly border.

Any pigmented moles of a dark color which have been irritated always arouse the physician's and the patient's fear of melanoma, but these can usually be readily differentiated from such by the absence of any change in surface markings and the absence of a smooth, nodular growth in or at the margin of the mole. Hairy moles very rarely become carcinomatous.

The pathological diagnosis of tissue suspected to be melanotic is sometimes just as difficult to make as is an exact clinical diagnosis. I have, on more than one occasion, known several of our most able pathologists to differ as to whether the sections showed benign or malignant pigmented growth.

For example, not long ago, I was asked to see a boy of 11 with a bathing-suit type of deeply brown pigmented hairy nevus covering

most of his trunk. A biopsy had been taken of the nevus when he was an infant and again two years later, and both specimens were reported by the pathological department of a well-known medical school as melano-carcinoma. In the meantime, the boy had developed normally and was strong and healthy in every way. Specimens of the growth were submitted to the pathological department of a local medical school, where the diagnosis of melano-carcinoma was confirmed. When the boy was presented to the New York Dermatological Society, the concensus was that the boy had only a bathing-suit type of hairy nevus.

From instances like this it becomes apparent that we must correlate our clinical findings with those of the laboratory in order to arrive at a correct conclusion.

Prevention of Epitheliomas: In order to safeguard against the formation of these cancerous skin lesions, we must recognize the condition under which such growths develop. Age; sex; color; exposure to the elements; scars from burns (particularly from radiation); keratoses, (both of the senile and seborrheaic varieties and those caused by arsenic); cutaneous horns; chronic ulcers, and trauma may all be contributing factors in the development of carcinoma.

While epithelioma may occur at almost any age, the great majority of such lesions are found in people over forty; Elliott and Welton[1] found that of 1742 cases of epithelioma, 27.7 per cent were in patients between the ages of 50 and 59—almost the same proportion reported by Ziesler,[2] 123 out of 461 were between the ages of 51-60. As age increases, the incidence of epithelioma increases.

Cancer is more commonly found in men than in women; of Elliott and Welton's 1742 patients, 57.4 per cent were male and 42.6 per cent were female.

The color of one's skin is an important factor in the development of cancer. The fair blond type which sunburns and freckles easily is especially apt to be subject to such growths of tumors. It is interesting that carcinoma is frequently found in the white areas of Hereford cattle, and on the white lids of the Longhorn Texas cattle. The darker the skin, the less likely one is to have cancer of the skin; for example, it is exceedingly rare to find a skin cancer in one of the Negro race.

Exposure to sun over a long period of time is believed to be one of the chief factors in producing skin cancers. In the Southern states the incidence of cancer on the exposed parts in individuals in rural sections,

especially farmers, is very high. Every spring I have a number of patients returning with deeply tanned skins from a winter in Florida, who come in with keratoses and skin cancers, chiefly on the face. Dr. Robert R. M. McLaughlin, in a personal communication, stated that the incidence of cancer in young men in the service who had been stationed in the South Pacific was frequent, particularly cancer of the lips. Sigmund Peller,[3] of Johns Hopkins University, and Charles S. Stephenson, of the U. S. Navy, found that skin and lip cancer occurred eight times more frequently in males in the U. S. Navy than in civilian population in same age group.

Lt. Commander G. A. Robinson,[4] in charge of the Radiology and Tumor Service, U. S. Naval Hospital, Long Beach, California, states that the incidence of keratosis and epithelioma in young naval personnel on South Pacific duty was very great. He states that blisters, fissures and hyperkeratoses precede cancer of the lip. The term "South Pacific" lip has been given to these lesions.

Skin cancer in old x-ray burns is very common. I have found that the probability of cancer increases with the age and the severity of the burn, and I believe that in 80-85 per cent of those having x-ray burns, a skin cancer will develop within 20 to 25 years, if the burn is on the exposed parts.

Skin cancer is also found sometimes in the scars of burns from other sources, particularly if the scars are in areas easily or frequently irritated. Most of us are aware of cancer at the site of pressure of glasses on the bridge of the nose, and from senile keratoses and so-called "liver spots," which appear on the face from age plus exposure.

Seborrhea, with a chronic scaling and a redness of the eyebrows and the groove between the wings of the nose and cheeks, often results in epithelioma.

Practically all patients with Xeroderma pigmentosa develop skin cancer on the exposed parts, particularly the face. Keratoses and cornified warts caused by arsenic frequently become carcinomatous, usually of the squamous cell type. These are not to be confused with the multiple superficial basal cell epitheliomas, which appear on the trunk—these also are attributable to arsenic.

Chronic ulcers of long standing, such as those due to tuberculosis, trophic ulcers, ulcers in sclerodermiac conditions—and, rarely, varicose leg ulcers may be the site of squamous cell carcinoma. Cutaneous horns

usually become carcinomatous and often of the metastasizing variety.

When we analyze the foregoing facts it immediately becomes evident that one must protect the aging skin by the exercise of proper hygiene, which consists of a thorough cleansing of the skin with water, washcloth and a fatty soap (cold cream, Castile or lanolin soap), the use of a suitable cream several times a day and the application of a protective, bland powder. It is imperative that the skin be protected from overexposure to sun and winds.

It has been my observation that the women who spend a great deal of time on the care of their complexions and hands rarely, if ever, are troubled with skin cancers or pre-cancerous conditions. Too, in this day of constant smoking—even by women—it may be that the protecting lipstick accounts for the infrequency of cancer of the lip in women.

The greatest safeguard against the development of cancers in x-ray burns is the excision of the scar where it is possible. Large areas which cannot be treated surgically should be kept carefully cleaned with fatty soaps and creams, as suggested above for senile skins. In addition, all keratoses and dilated blood vessels should be removed by the electric needle, thereby reducing the development of cancer in these burned areas.

Every endeavor should be made to heal all chronic ulcers. Scars should have gentle massage with cream, and, where possible, tension and all friction of scars should be eliminated. Senile keratoses, collections of dilated blood vessels and all arsenical keratoses should be removed, preferably with the electric needle, in order to safeguard the skin against cancer.

Treatment: Practically 100 per cent of all skin cancers of the basal and squamous cell variety can be cured if removed early in their development, regardless of the method of treatment employed—provided it is *thorough*. Undoubtedly there are some lesions better suited for treatment by one procedure than by another, but I have always considered the choice of the method secondary to that of the thoroughness with which it is done. Tragedies resulting from basal and squamous cell carcinoma of the skin are always due to neglect or to inadequate treatment. Each time a skin cancer recurs after removal the greater the difficulty of treating it successfully. Furthermore, the chronic irritation oftentimes produced by improper treatment of a basal cell epithelioma produces an additional skin cancer of the squamous or metastasizing

type, so that the patient has two growths to contend with, and he is in a much more serious condition than he would have been without treatment.

To illustrate, a few years ago a well-known surgeon brought me a patient with inoperable carcinoma of the skin, who had been through successive methods of treatment for eleven years. The lesion had begun as a small, wartlike keratosis just above the right eyebrow—this the Doctor had curetted and cauterized. When the lesion recurred six months later it was taken off with an electric needle. The third recurrence was treated by a radiologist with radium. The fourth was treated at a well-known cancer hospital, where he had an operation, followed by radiation. Later he spent some time in Paris, and was treated with radium at the Curie Institute. He then returned to New York and consulted an eminent cancer expert at a cancer hospital. Both in Paris and in New York the doctors assured him that sequestra of bone, which came out of the superorbital wound, was due to the necrosis of the bone from radium, and that he had no cancer. The lids of the right eye were closed with a dark red, firm, brawny swelling, and a pencil could be introduced an inch or more into the hole beneath the right eyebrow. Red, granular, warty tissue was around the ulcer. The diagnosis of carcinoma was obvious, and a radical surgical operation was advised. Of course, the primary lesion was only a keratosis which could have been effectively and easily removed if it had been done thoroughly.

I see so many instances of a similar character that I have become convinced that the average physician regards cancers and pre-cancerous conditions of the skin too lightly, and does not treat such lesions thoroughly enough. The foremost consideration of every physician should be the complete removal of every cancerous growth, regardless of the resulting scar. For many years I have made it a practice to remove skin cancers with the electric needle, first taking a piece for biopsy study, then following with thorough desiccation of the lesion and beyond the border, removing the charred or desiccated material with a curette or scalpel. I repeat this procedure until I feel I have gone well beyond the diseased borders. I then give 1800 R in three divided doses.

My results in cases which had had no previous treatment have been, so far as it has been possible to follow, approximately 100 per cent successful, as far as a return of the growth is concerned.

Elliott and Welton treated 1052 cases of basal and squamous cell

carcinoma—some without previous treatment and others with—using the combined method of the electric needle, curettage and radiation, and they report that 97.1 per cent had cures for five years or longer. That is a remarkable and encouraging result.

Treatment of Melano-Carcinoma: The best protection against melano-carcinoma is to remove thoroughly all pigmented moles situated at sites where they might be subjected to irritation. This removal can be accomplished safely with the electric needle.

The only cases of metastatic melano-carcinoma arising from moles which I have seen have followed either surgical excision or cauterization with acids. For example, a thirty-six year old physician consulted me, stating that six months previously a surgeon had excised a dark colored mole from the back of his right shoulder. A few months later a walnut-sized gland appeared in the right axilla following a few days of strenuous golfing. He had had fever 102°, general malaise and considerable discomfort in the swollen gland. He was relieved of his discomfort in twenty-four hours by radiation, his gland subsided to almost normal and his temperature fell. Within three weeks two or three hazelnut-sized glands were felt in the same axilla; biopsy of one showing melano-carcinoma.

Any blue nodule or papule in the skin, of recent development, should be deeply and widely excised at the earliest possible opportunity. Even then it is doubtful that metastasis may be prevented, and especially is this true of lesions which may appear on the buttocks, the sole of the foot, around the nail or on the glans penis, as I saw in a case a few weeks ago. Metastasis in such cases takes place early, possibly with or even before the appearance of the nodule. The prognosis of melanoma in infancy or childhood is much more favorable.

Summary: The prevention of epitheliomas is best accomplished by exercising proper care of the skin; by removing all known irritants which give rise to some pre-cancerous condition; by avoiding continuous or over exposure of the skin to the sun or sun lamps; by careful treatment of x-ray burns, keratoses of all types; by avoiding long and excessive use of arsenic compounds.

Epitheliomas of the skin can be successfully removed if treated early enough and with thoroughness. The selection of the method of removal is secondary to the complete eradication of all cancerous growth.

All pigmented moles which show changes in surface markings, or

become irritated, or are situated in locations likely to be subjected to irritation should be removed carefully and completely, preferably with the electric needle.

Melano-carcinomas must be removed immediately by wide and deep excision.

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Candidates must be physicians, who have been graduated at least three years and are residents of the United States. Candidates shall submit evidence of research, already performed and of facilities to prosecute research upon the causation, pathology and new methods of treatment of diseases of the kidney.

Applications, with the required evidence, should be addressed to The Gibbs Prize Committee at The New York Academy of Medicine, prior to March 31.